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LabLink

Director, Bureau of Laboratories
Sandip Shah, Ph.D., HCLD(ABB)

this issue...

Bureau Vision

The Bureau of Laboratories is a stronger, more diverse team within an integrated public health system. We utilize advanced technology and innovative leadership to provide comprehensive public health services in our dynamic global community.

Bureau Mission

We are dedicated to continuing leadership in providing quality laboratory science for healthier people and communities through partnerships, communication and technical innovation.

CAP ACCREDITED

MDHHS
Michigan Department of Health & Human Services
RICK SNYDER, GOVERNOR | NICK LYON, DIRECTOR

New State-Wide Courier Service Launched in 2017

Author: Martha Boehme, Quality Assurance Section Manager

January 3 not only started the New Year, but also saw the introduction of STAT Courier Service, Inc. as the new provider of transport services for specimen delivery to the state public health laboratory.

This was a big transition for the laboratory after more than a decade of outstanding service from Quest Diagnostics and more recently, from A-1 International couriers. Both companies were valuable partners as the service grew from limited clinical specimen transport in 2003 to the inclusion of 76 hospital birthing center pickups 6 days a week. We rely heavily on contracts with these private sector partners to pick up and deliver nearly 125,000 newborn screening specimens per year, along with thousands of infectious disease specimens to our laboratory for testing.

The transition went very well; and we are grateful to all of our public health and laboratory system partners for their patience and cooperation as we worked through the inevitable bumps in the road that accompany any major change.

The state laboratory is able to subsidize some of these expenses through a combination of laboratory service fees and federal cooperative agreements. We also provide paid UPS return service for some of our more time-sensitive specimens from many sites that do not receive courier service.

Getting specimens to Lansing for testing is a complicated process and involves many players. We welcome your feedback and suggestions as we look for ways to improve our services in 2017.

BOL Introduces Our New Laboratory Systems Section, Outreach Departmental Analyst

The Bureau of Laboratories would like to introduce Sandra Lenneman as our most recent appointee to the Laboratory Systems Section.

Sandy has accepted the Department Analyst position responsible for maintenance of the Bureau's "Exp!ore Lab Science" outreach educational program and as support for the Bioterrorism Training Coordinator and the Chemical Threat Response Training Coordinator. Sandy began her duties on Monday, November 7, 2017.

Sandy comes to us with many years of experience from working at the American Red Cross. She served as the liaison for the American Red Cross and approximately 40 hospitals for account management of blood products and services, transfusion medicine education programs, and contract negotiations. She has experience with policy and procedure development, problem solving, quality improvement plan development, application, and analysis, customer relations and production and implementation of educational programs.

Sandy has earned an Master of Sciences and Health Services Administration from Central Michigan University, and a Bachelors of Science in Medical Technology from Michigan State University.

Welcome Sandy!

Michigan Department of Health and Human Services Bureau of Laboratories

Welcomes New Chemistry and Toxicology Division Director

Please welcome Dr. LiSheng Chen as the new Division Director of Chemistry and Toxicology at the Michigan Department of Health and Human Services Bureau of Laboratories (MDHHS BOL). Dr. Chen is certified as a Diplomate of the American Association of Clinical Chemistry. We welcome her wealth of knowledge and experience in clinical chemistry.

Dr. Chen began her career as a medical technologist in Taiwan. Upon arrival to the United States, she obtained her PhD and received clinical training at Mayo Clinic. She was a junior faculty member in the Department of Pathology at the University of Rochester Medical Center, where she was appointed Associate Director of Automated Laboratory for five years.

In addition, Dr. Chen served as a Staff Fellow at the Food and Drug Administration (FDA) in the Office of *In Vitro* Diagnostics, where she specialized in reviewing assay and instrument submissions, and formulating related regulatory guidance and policies. She worked as Laboratory Director for a start-up diagnostic company responsible for initiating mass-spectrometry based multiplex pharmacogenomics testing for two years prior to joining the MDHHS BOL.

Dr. Chen would like to work with laboratory colleagues and collaborate with our clinical partners at local, state, and federal agencies in order to provide the highest quality of laboratory testing for our public health partners and Michigan residents.

Please feel free to contact Dr. Chen regarding any issues related to the Newborn Screening and Analytical Chemistry laboratory testing programs. She can be reached at (517) 335- 9490.

Michigan Department of Health and Human Services Bureau of Laboratories Announces Interim Infectious Diseases Division Director

The Bureau of Laboratories is extremely pleased to announce the appointment of Marty Soehnlen, PhD, as the interim division director of Infectious Diseases Division.

Dr. Soehnlen began her laboratory career at Ohio State University where she received her Bachelors of Science in Medical Technology. The University of Michigan is where she obtained her Masters of Public Health degree in Hospital and Molecular Epidemiology with sub-specialization in public health genetics. While attending the University of Michigan her research was focused on glaucoma genetics.

Dr. Soehnlen was accepted by the Centers for Disease Control and Prevention (CDC) as an Association of Public Health Laboratories (APHL)/CDC Class XII Emerging Infectious Diseases (EID) Fellow with the Rabies section.

Dr. Soehnlen then chose to return to educational pathway for her PhD; this time at Pennsylvania State University studying Pathobiology. Her dissertation work was entitled “Molecular Characterization and Epidemiology of *Mycoplasma bovis*”. Dr. Soehnlen accepted a post-doctoral fellowship through the Oak Ridge Institute for Science and Education (ORISE) which located her in Landstuhl, Germany working alongside the United States (US) Army.

While she was in Germany, Dr. Soehnlen accepted a Department of the Army Civilian position as the Chief of Microbiology and Molecular Biology Division and Deputy-Chief of the Veterinary Pathology Division of the US Army Public Health Command Region Europe. Following her 4 years residing overseas, Dr. Soehnlen returned to the US and joined the Bureau of Laboratories as the Manager of Microbiology Section in April, 2015.

Please welcome Dr. Marty Soehnlen in her new interim position which started on December 18, 2016. Please feel free to contact her regarding any issues related to Infectious Diseases laboratory operations and testing by telephone or email at:

(517) 335-8064 or soehnlenm@michigan.gov.

LABORATORY GUIDANCE FOR ZIKA VIRUS TESTING—12/08/2016

Testing at the Michigan Department of Health and Human Services—Bureau of Laboratories

Author: Janice Matthews-Greer, PhD, (DABMM) Section Manager, Virology & Immunology , Division of Infectious Diseases

OVERVIEW

On November 28, 2016, Texas Department of State Health Services and Cameron County Health and Human Services in the Brownsville area, announced the first case of Zika virus disease likely transmitted by a mosquito in Texas. Local and state public health officials are responding with additional human and mosquito surveillance in the area around the patient's home and are offering educational support to neighbors about risk mitigation of Zika and tips for elimination of mosquito habitat on their property. This adds Texas, alongside Florida, to the list of states within the United States (US) with locally-acquired, mosquito-transmitted Zika infection.

As of December 28, 2016, the number of Zika virus disease cases in the US reported to ArboNET is 4,809; 216 of these were locally-acquired. Michigan ranks 13th in the number of cases per state with 69 cases detected by the end of 2016. Total reported cases in the US Territories by the end of 2016 were 35,152, with >99% being locally-acquired. As of mid-December, 1,246 pregnant women with any lab evidence of Zika virus infection were reported in the US with 2,842 cases in US Territories. (These are the numbers recorded in their respective pregnancy registries.) By the end of 2016, in the US, five pregnancy losses and 36 live-born infants exhibiting birth defects, had been reported. Birth defects detected include microcephaly; calcium deposits in the brain indicating possible brain damage; excess fluid in the brain cavities and surrounding the brain; absent or poorly formed brain structures; abnormal eye development; or other problems resulting from damage to the brain that affects nerves, muscles and bones, such as clubfoot or inflexible joints; and confirmed hearing loss. Thirteen US and 50 US Territory cases of Guillain-Barre' syndrome are reported.

ZIKA SCREENING

Specimens collected from patients meeting the Centers for Disease Control and Prevention (CDC) clinical and epidemiological criteria should be tested for Zika virus RNA or IgM. **Top priority for public health's response to Zika infection is to protect pregnant women and their unborn babies**. Therefore, testing is focused primarily on pregnant women at risk, i.e. those who live in, have traveled to, or had unprotected sex with someone who traveled to an area known to have locally-transmitted Zika disease. Pregnant women at risk and symptomatic individuals (men and women) are screened for Zika if the timing falls within the CDC guidelines described below and illustrated in Figures 1-3. Areas with active Zika transmission can be found at the CDC website: http://www.cdc.gov/zika/geo/index.html.

Couples planning to conceive should consider avoiding travel to areas with local Zika virus transmission. Women who are exposed to the virus through travel or unprotected sex with a partner who has traveled to an area of risk should consult with their healthcare providers. Current recommendations from the CDC are to postpone conception for at least 8 weeks from symptom onset or last possible exposure to Zika. Men should avoid attempting conception for at least 6 months from symptom onset or last possible exposure. **The Bureau of Laboratories (BOL) cannot test women or men for purposes of family planning or to see if an individual is Infectious.** This should be discussed with their primary healthcare provider.

Serum and urine are the primary diagnostic specimens for Zika virus screening and diagnosis. Other specimen types such as plasma, whole blood, cerebrospinal fluid (CSF), and amniotic fluid are authorized for use with some Zika RT-PCR RNA tests that have received a Food and Drug Administration (FDA) Emergency Use Authorization (EUA). All specimens *must* accompany an additional "paired-serum" sample (an extra tube of serum drawn at the same collection time). This extra serum sample is necessary for PCR and reflex IgM testing.

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NOTE: The MDHHS BOL ***cannot*** accept plasma or whole blood at this time. We request **two vials of serum** and one vial of urine. If CSF or amniotic fluid is submitted, please submit in 1 mL aliquots.

IMPORTANT: Please be especially careful when **labeling specimen vials** for submission as "urine" or "serum" as these two specimens can look identical.

Screening for Zika virus infection is outlined as described below. Algorithms for these testing recommendations, based upon the most recent CDC Guidelines, **Figures 1-3**, are located on pages 12-14.

- For ***SYMPTOMATIC pregnant* patients** with exposure to Zika virus, **RNA** nucleic acid testing (NAT or **PCR**) of **serum and urine** is recommended **up to 2 weeks after symptom onset.** If negative, serology is performed. (See Figure 1)

- RNA testing of **serum and urine** is recommended
  - ***a)*** **< 2 weeks after the last possible exposure** for ***ASYMPTOMATIC pregnant* women** who live in areas without active Zika virus transmission
  - ***b)*** for those who are **evaluated 2-12 weeks after exposure** and have been found to be Zika virus ***IgM-positive.***

- For ***ASYMPTOMATIC pregnant* women**, within **2-12 weeks after the last date of possible exposure** and who live in areas without active Zika virus transmission, **RNA** testing of **serum and urine** is recommended **up to 2 weeks after the last possible exposure** and for **those evaluated 2-12 weeks after symptom onset**, if they have been found to be Zika virus ***IgM-positive***.

- ***ASYMPTOMATIC pregnant women,*** with exposure to Zika, may be offered screening with **serologic testing** within **2-12 weeks after the last date of possible exposure**.

- ***ASYMPTOMATIC pregnant*** women, who live in areas with **active Zika virus transmission,** should have Zika virus **IgM testing** as part of routine obstetric care during the **1st and 2nd trimesters**, with **immediate RNA** testing of women who are **IgM-positive**: A positive RNA NAT test provides a definitive diagnosis of Zika virus infection.

- ***NEWBORNS* should be tested within 48 hours of birth** by RT-**PCR** of serum and urine, plus **IgM** capture for Zika infection and testing is recommended for
  - ***a)*** infants born to **mothers with laboratory evidence*** of possible Zika virus infection
  - ***b)*** infants with **signs of congenital Zika**** syndrome at birth or for
  - **c)** infants with a ***mother at risk*** from living in or traveling to an area with Zika, or had sex with a partner who lived in or traveled to an area with Zika (without barrier method protection to prevent infection)

  NOTE: In each case, testing the **placenta** by RT-PCR should be considered if the status of the mother is uncertain.

* If maternal samples are collected around the time of delivery, which is >12 weeks after symptom onset or exposure, infant samples should be collected. If maternal IgM is negative, infant testing should be considered, because a negative IgM result does not rule out recent maternal Zika virus infection. If maternal IgM is positive or equivocal, infant testing should be based on maternal PRNT results (if neutralizing antibodies to Zika are detected, infant testing should be pursued).

** Microcephaly at birth is not a necessary feature of congenital Zika syndrome. Infants with a head circumference in the normal range at birth can have brain abnormalities consistent with congenital Zika syndrome. In addition, microcephaly from congenital infection can develop after birth.

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Zika Testing Guidance, continued from Page 6

OTHER VIRUSES CAUSING ZIKA-LIKE SYMPTOMS

It is important to note that Zika virus infection can cause signs and symptoms similar to those seen in patients with other arthropod-borne virus (arbovirus) infections, including dengue virus, a related flavivirus, and chikungunya (CHIK) virus, an unrelated alphavirus. Also a positive result for one of these viruses does not preclude infection with the others. Co-infection with Zika virus and dengue or CHIK virus is rare, but we have seen it here in Michigan. Several single infections with CHIK and many cases of dengue have been found by BOL Zika testing section. For this reason, the BOL tests for all three arbovirus infections, Zika, dengue and chikungunya, by both PCR and IgM capture ELISA. Remember that chikungunya is a BSL-3 agent, and the viral loads for CHIK in positive specimens are extremely high. Based upon a complete risk assessment, Zika virus serology testing at the BOL is performed in a BSL-2 laboratory with BSL-3 practices. Pregnancy should be considered a significant factor in risk assessment for individuals working with Zika virus, and the involvement of pregnant workers should be kept to a minimum.

ZIKA RT-PCR: TESTING AND SPECIMENS

The first marker of Zika infection is **RNA** detectable PCR (RT-PCR, NAT.) PCR can be positive in the **serum** 24 hours (or less) after the onset of symptoms and usually remains detectable for 7-10 days. **Urine** and **saliva** can also be RNA-positive shortly after the onset of symptoms, but can remain positive for a longer period of time – up to 2 weeks. In pregnant women, viremia can last longer (detectable RNA in serum 107 days after symptoms, presumably from the infected fetus, have been reported).

Recently **whole blood** has been cited as the most sensitive sample for RT-PCR, but not all laboratories have the automation required by the CDC's standard operating procedure for whole blood extraction under the Emergency Use Authorization (EUA). Make sure the lab you are using can perform testing on the sample type you submit. **The BOL does NOT accept whole blood, plasma, semen, or saliva routinely at this time**. **Cerebrospinal fluid** (**CSF**), **amniotic fluid**, and **placenta** can also be submitted for Zika RNA detection: The placenta will be forwarded to the CDC. The BOL performs the CDC Trioplex RT-PCR, a multiplex assay that detects RNA from Zika, dengue and/or chikungunya viruses.

All positive PCR results are final and do not need to be confirmed. Negative results are reflexed to serology. **For this reason ALL specimens submitted for Zika testing must be accompanied by serum**.

Multiple nucleic acid tests have received EUA from the FDA. The FDA maintains a list on its website of all Zika virus EUAs. Please refer to the FDA website for a current list of available assays and associated letters of authorization, fact sheets, and product labeling. Additional assay-specific information (e.g., performance characteristics) is included in the labeling. Information about molecular tests that have been cleared by FDA for detection of arboviruses other than Zika virus can be found in the FDAs searchable database (http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/510kClearances/ucm089319.htm).

ALTERNATIVE SPECIMENS:

Cerebrospinal Fluid: Cerebrospinal fluid is not a primary diagnostic specimen for Zika virus testing. However, if CSF is obtained during evaluation for other reasons, the specimen may be tested for the presence of anti-Zika IgM antibodies by ELISA, for the presence of Zika virus RNA by the Trioplex, and possibly other molecular methods. CSF, along with paired serum specimens, should be tested by Zika RNA NAT if collected <14 days following onset of symptoms. CSF and serum should be tested by antibody detection methods if collected >14 days after symptom onset, or if PCR is negative in samples collected <14 days after onset of symptoms.

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Amniotic Fluid: If indicated, amniotic fluid may be tested by Trioplex and possibly some other EUAs, alongside paired serum and urine specimens. Consideration of amniocentesis should be individualized, because data regarding sensitivity and specificity of Zika virus testing at different time points during pregnancy to diagnose congenital Zika virus infection are limited. The presence of Zika virus RNA in the amniotic fluid might indicate fetal infection; however, a negative result does not exclude congenital Zika virus infection.
Please see Oduyebo et al, 2016 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6529e1.htm?s_cid=mm6529e1_e), for additional information regarding testing of amniotic fluid.

Tissue Specimens: There are currently no FDA authorized tests for Zika virus testing of tissue specimens; however, Zika, dengue, and chikungunya virus testing on fixed and frozen tissue at the CDC may be considered on a case-by-case basis: Fixed tissues are preferred. Requests for testing should be coordinated through the BOL or local/state health departments; pre-approval is required before submission to the CDC. Additional information about specimen collection and submission procedures is available on the CDCs website : (https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html).

CDC MAC ELISA FOR ZIKA IGM TESTING

Fact Sheet for Patients
http://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM488042.pdf

IgM rises after RNA, generally at 4-5 days and lasts for 12 weeks in most individuals, ranging from 8-12 weeks. It may be missed in specimens drawn <4 days from the onset of symptoms. **Therefore, if the IgM is drawn early and yields a negative result in a pregnant patient or her partner who exhibits the symptoms of Zika infection, an additional serum specimen should be drawn and submitted at a later date. Please note on the tube that this is a pregnancy follow-up serology for Zika.** Some laboratories use alternate EUA IgM test kits for detecting Zika IgM. Check to see if serum or plasma is preferred. The BOL requires serum. For whatever test is performed, a confirmation plaque-reduction neutralization assay (PRNT) is required if the result is positive or equivocal for Zika IgM. Sera are sent either to the CDC or if the patient is a Michigan resident, to the BOL for PRNT confirmation. A negative Zika IgM is final. (Note when a follow-up specimen is recommended.)

Because infections with other arboviruses, including chikungunya virus, can also produce symptoms similar to Zika virus infection, often additional testing for other arboviruses is required to reach a diagnosis. For persons with chikungunya exposure risk and a clinically compatible illness, anti-chikungunya IgM testing should also be performed. The BOL also tests for dengue virus in all specimens submitted for Zika virus testing.

ZIKV DETECT™ IGM CAPTURE ELISA: INBIOS INTERNATIONAL, INC.

On August 17, 2016, FDA issued EUA for use of InBios International, Inc.'s ZIKV Detect™ IgM Capture ELISA for the presumptive detection of Zika virus IgM antibodies in human sera. This is the first commercially available serological test for Zika available under EUA: The first serological test, the CDC Zika MAC-ELISA, was initially authorized for use in February 2016. This test is intended for use with human sera collected from individuals meeting the CDC Zika virus clinical criteria (e.g., a history of clinical signs and symptoms associated with Zika virus infection) and/or the CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated).

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Zika Testing Guidance , continued from Page 8

Where there are presumptive Zika positive, possible Zika positive, or presumptive other flavivirus positive results from the ZIKV Detect™ IgM Capture ELISA, confirmation of the presence of anti-Zika IgM antibodies or other flavivirus IgM antibodies requires confirmation at the BOL. Please refer to the authorized "Instructions for Use" document, using the latest CDC guideline for the diagnosis of Zika virus infection. **Please note that the different ZIKA IgM-MAC-ELISA tests, CDC and InBios, can result in discrepant results. This is the subject of a recent BOL HAN (1-5-2017) regarding the FDA cautionary report.**

PRNT TESTING

Currently, within the United States, when ELISA IgM antibody testing indicates the presence of anti-Zika IgM antibodies (positive, equivocal, presumptive or possible Zika virus positive result), PRNT, which measures virus-specific, neutralizing antibodies to Zika virus and other endemic flaviviruses, is required for diagnosis. PRNT must be conducted by the CDC or a laboratory qualified by the CDC.

PRNT is available at the BOL. We have agreements with several reference laboratories to receive all specimens from Michigan residents who require Zika IgM confirmation testing.

If ELISA testing indicates a positive or equivocal result for dengue infection, confirmatory testing should be performed as indicated in the IgM assay labeling. Given the high degree of antibody cross-reactivity observed with Zika and dengue infections, results of Zika/dengue PRNT testing should be interpreted alongside initial IgM assay results to assess the status and timing of infection. The CDC Interim Guidance for Interpretation of Zika Virus Antibody Results contains specific information that guides the overall interpretation of combined results from Zika virus and dengue virus ELISA and PRNT. Rabe et al., 2016, https://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm) Unfortunately, PRNT is not always able to provide a definitive determination of the specific flavivirus causing a recent infection, particularly in persons with a prior history of flavivirus infection. For this reason, PRNT confirmation at current is not routinely recommended in Puerto Rico, where dengue virus is endemic and cross-reactivity is likely to occur in most cases. ***Box A*** lists final results possible from PRNT testing for Zika.

ADDITIONAL COMMENTS

It is important to note that serum is required for all diagnostic algorithms and thus a paired serum specimen must be submitted alongside all other sample types.

BOX A
POSSIBLE PRNT FINAL RESULTS

Recent Zika virus infection†
Recent dengue virus infection†
Recent flavivirus infection; specific virus cannot be identified†
No evidence of Zika virus or dengue virus infection
Evidence of Zika virus infection; timing cannot be determined§
Evidence of dengue virus infection; timing cannot be determined§
Evidence of flavivirus infection; specific virus and timing cannot be determined§
Presumptive recent Zika virus infection†,§
Presumptive recent dengue virus infection†,§
Presumptive recent flavivirus virus infection†,§
Equivocal results§
Inconclusive results§
No evidence of recent Zika virus or dengue virus infection

*For persons with suspected Zika virus disease, Zika virus RNA NAT should be performed on specimens collected <14 days after onset of symptoms.

†In the absence of RNA nucleic acid testing, negative IgM or neutralizing antibody testing in specimens collected <7 days after illness onset might reflect collection before development of detectable antibodies and does not rule out infection with the virus for which testing was conducted.

§Zika IgM positive result is reported as "presumptive positive" to denote the need to perform confirmatory PRNT. Report any positive or equivocal IgM Zika or dengue results to state or local health department.

**To resolve false-positive results that might be caused by cross-reactivity or nonspecific reactivity, presumptive positive Zika IgM results should be confirmed with PRNT titers against Zika, dengue, and other flaviviruses to which the person might have been exposed.

Adapted from CDC Interim Guidance for Interpretation of Zika Virus Antibody Results (Rabe et al., 2016).

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Note to Healthcare Providers: *To determine which specimen types can be tested and for specific specimen collection, handling and storage requirements, please consult the testing laboratory or the labeling information for current tests with Emergency Use Authorization.*

Note to Healthcare Providers: *Please **do not submit urine in urine collection cups** for Zika virus testing. Urine should be transferred to a **clean vial with screw cap and O-ring** to prevent leakage in transport. (See **Box B** below).*

Note to Healthcare Providers: *Prior approval from your local health department or a state epidemiologist is **NO LONGER** required. A **new** Michigan Zika Supplemental Questionnaire is required (See **Box C** below). It must be filled out completely and sent with the patient specimens to the BOL. Only those patients falling within the timeline recommended by the CDC Guidelines will be tested.*

***Testing Infants**: If the infant's initial serum sample is negative for RNA but is IgM-positive, then PRNT should be performed on the infant's initial sample if it was not performed on the mother. However, **PRNT cannot distinguish between maternal and infant antibodies at birth**. For infants with an initial sample that was negative for Zika virus RNA, serologic testing (IgM followed by PRNT if indicated) at ≥18 months of life, when maternal antibody has waned, can assist with diagnosis for congenital Zika virus infection.*

BOX B

SPECIMENS AND VOLUMES REQUESTED FOR ZIKA TESTING

2 mL serum for RNA + 2 mL serum for IgM + 2 mL urine for RNA

Always include a urine and two tubes of sera just in case the sample is reflexed for additional tests.

Serum MUST be submitted regardless of other sample types submitted.

Ship specimens on a frozen ice pack using screw-capped tubes with O-rings.

These shippers are available from the BOL by calling Mark Warstler at 517-335-9037 or by email at warstlerm1@michigan.gov

BOX C

MANDATORY PAPERWORK FOR SPECIMEN SUBMISSION

Patient History Form (Michigan Zika Supplemental Form) COMPLETELY Filled out

BOL Requisition Form – 1 for each specimen source:

http://www.michigan.gov/documents/DCH-0583TEST_REQUEST_7587_7.pdf

http://www.michigan.gov/documents/mdhhs/MichiganZikaSupplementalQuestionnaire_5-5-2016_003_524044_7.pdf

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TESTING ALGORITHMS FOR DETECTION OF ZIKA VIRUS INFECTION

Testing algorithms (**Figures 1, 2 and 3**) were designed to accommodate the temporal nature of the appearance and disappearance of markers of Zika virus infection and to optimize testing for pregnant women**.**

Figure 1: For **symptomatic** patients with specimens collected at **<14 days post-onset** of symptoms or post-exposure, test serum and urine with a Zika virus RNA NAT. (A RNA-positive Zika virus NAT result in *any* specimen is sufficient to diagnose Zika virus infection.) If Zika virus RNA NAT results are negative, serum should be tested for the presence of anti-Zika IgM. A reactive (Equivocal, Presumptive Positive or Possible Zika Positive) anti-Zika IgM result is followed by PRNT to confirm the diagnosis.

Figure 2: If specimens collected at **≥ 14 days** are Zika IgM equivocal or positive, and the patient is **pregnant**, perform RT-PCR prior to PRNT confirmation.

Figure 3: If specimens collected at **<14 days post-exposure** are IgM negative by anti-Zika IgM and the patient is **pregnant**, recollect serum at a later date (2-12 weeks post exposure) and perform serology testing, including PCR on all IgM-positive or equivocal specimens prior to PRNT confirmation. (In this last case, the BOL performs serology on the specimen collected at <14 days, as well as asking that another specimen collected at 2-12 weeks be submitted for repeat serology, just in case a mother can be diagnosed at an earlier date.)

REPORTING

Each test result generated for each specimen should be reported to clinicians as specified in the assay instructions for use. Pregnancy status should also be reported to allow health care providers to readily identify these women. Results generated by methods used under FDA EUA must be accompanied by the appropriate fact sheets when reported back to providers and patients. Fact Sheets have been prepared for health care providers and patients to help each understand the results of testing. Authorized Fact Sheets for each assay under EUA are posted to the FDA website (http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm)

Please note that Zika, dengue and chikungunya virus infections are all on the 2016 list of nationally notifiable conditions (https://wwwn.cdc.gov/nndss/conditions/notifiable/2016/). Results of testing should be reported back to state or local health department staff to facilitate investigation and classification of the case and reporting to the CDC.

QUESTIONS

Should you have questions about Zika testing, please contact one of the following:

Janice Matthews-Greer, PhD, (DABMM)	**Virology & Immunology Section Manager:**	**517-335-5067**
Kristine Smith	**Immunology Unit Manager**	**517-335-9117**
Bruce Robeson	**Virology Unit Manager**	**517-335-8098**

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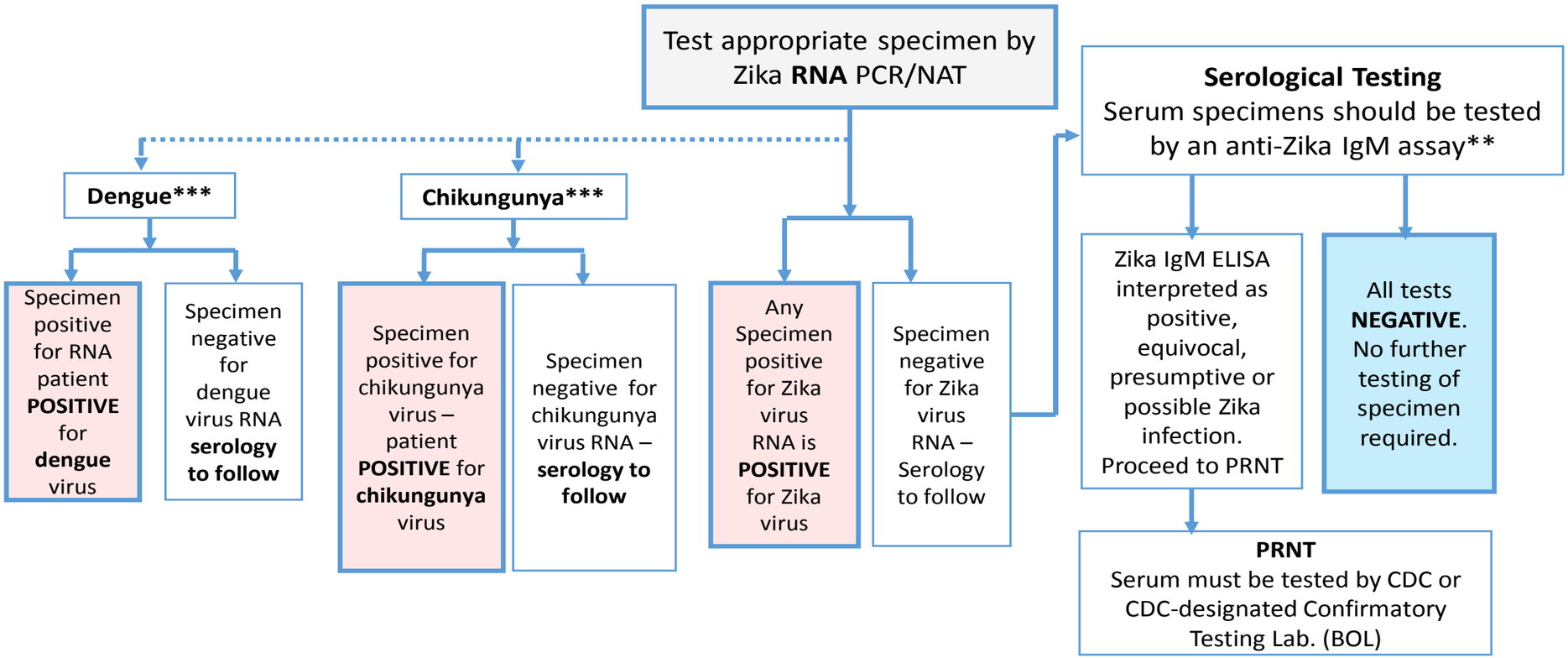
Fig. 1

2016 Zika Response: Algorithm for US Testing of *SYMPTOMATIC* Individuals*
Specimens collected *<14 days* Following Symptom Onset



NOTE: Report all test results. Results should be considered in the context of symptoms, exposure risk, and time point of specimen collection.
***Pregnant and non-pregnant symptomatic individuals**
**** Note antibody cross-reactivity to other flaviviruses complicates interpretation of the current anti-Zika IgM tests, Dengue IgM testing should be conducted for symptomatic pregnant women, individuals with a potential dengue exposure and when a presumptive other flavivirus result is obtained.**
***** Indicates testing and interpretation for the CDC Trioplex assay. Note when testing urine and amniotic fluid with the CDC Trioplex assay, only report the Zika result.**
+ PRNT confirmation is not routinely recommended for Puerto Rico.

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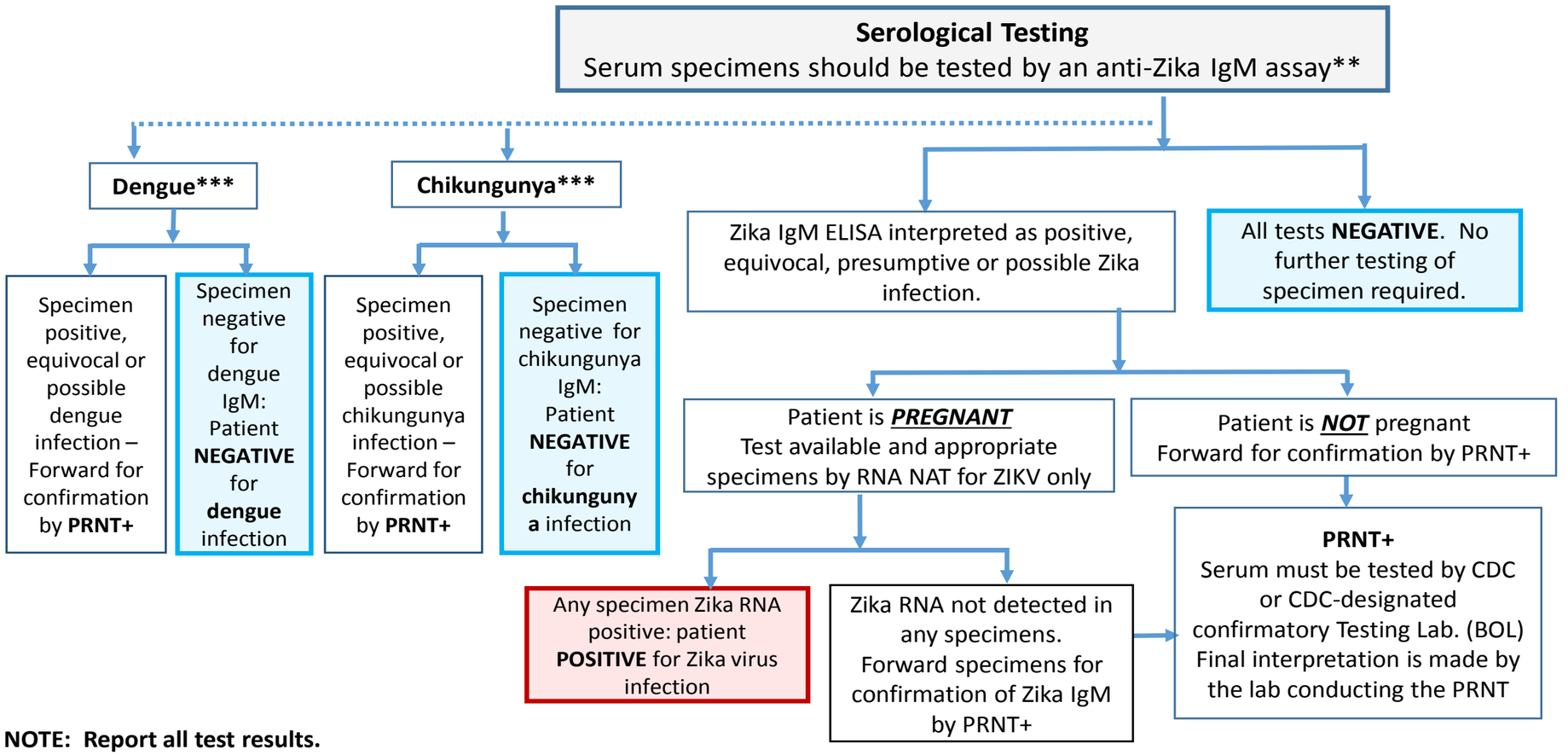
2016 Zika Response: Algorithm for US Testing of ***SYMPTOMATIC*** Individuals*
Specimens collected ***>14 days*** Following Symptom Onset

Fig. 2



NOTE: Report all test results.
Results should be considered in the context of symptoms, exposure risk, and time point of specimen collection.

***Pregnant and non-pregnant symptomatic individuals**

****** Note antibody cross-reactivity to other flaviviruses complicates interpretation of the current anti-Zika IgM tests, Dengue IgM testing should be conducted for symptomatic pregnant women, individuals with a potential dengue exposure and when a presumptive other flavivirus result is obtained.**

******* Note if tests for Zika and Dengue IgM are not reactive, anti-chikungunya IgM testing should be performed for persons with chikungunya exposure risk and a clinically compatible illness**

+ PRNT confirmation is not routinely recommended for Puerto Rico.

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Zika Testing Guidance , continued from Page 13

2016 Zika Response: Algorithm for U.S. Testing of *ASYMPTOMATIC PREGNANT* Women Meeting Epidemiologic Criteria

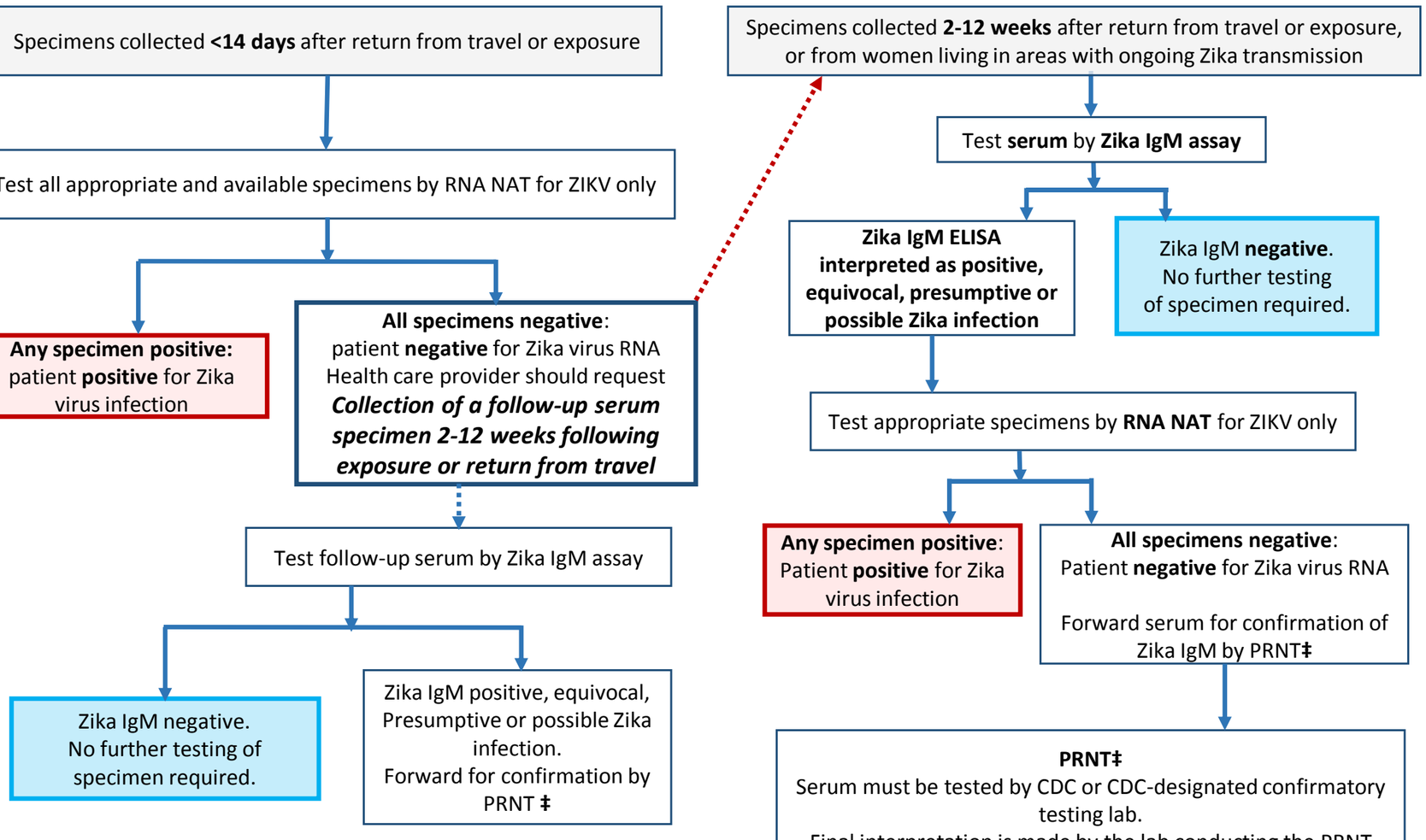

Fig. 3

NOTE: Report all test results to the appropriate Health Authorities. Results should be considered in the context of exposure risk and time point of specimen collection.
See this link for additional information for assessing epidemiologic risk: http://www.cdc.gov/zika/geo/index.html
‡PRNT confirmation is not currently routinely recommended for Puerto Rico.

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Editor: Teresa Miller